Data & Safety Monitoring Plan Guidance

Data and Safety Monitoring

For greater than minimal risk research, the IRB requires the investigator to have a Data and Safety Monitoring Plan in place that protects the safety of subjects, the validity of the data, and the integrity of the research study. The IRB reviews the plan and determines if the plan has adequate provisions in place for monitoring the data collected to ensure the safety of participants.

If the research is considered minimal risk, then the development of a data and safety monitoring plan may be helpful, but its development is not required by the IRB unless, the IRB determines a data and safety monitoring plan is needed for the oversight of the study.

When developing a DSMP, the investigator should take into account the risks of the study and provide an adequate plan to review study data in order to minimize those risks. The extent to which data are monitored should increase as the level of risk to participants increases. At a minimum, greater than minimal risk human subjects research studies should be monitored by the PI and IRB but could require additional monitoring by an independent safety monitor or Data Safety Monitoring Board (DSMB).

To that end, an investigator should consider the following elements when developing a protocol specific DSMP:

- **Subject Safety**: monitoring is conducted to avoid or minimize risks (i.e. physical, psychological or social).
- **Data Integrity**: monitoring is conducted to assure data is accurate and complete. Monitoring of data assures adherence to the approved clinical study.
- **Subject Privacy**: monitoring is conducted to assure individual's rights are protected.
- **Data Confidentiality**: monitoring is conducted to assure data is secured.
- **Product Accountability**: monitoring is conducted to assure drug(s) or device(s) are tracked and accounted for.
- **Study Documentation**: monitoring is conducted to assure that required documentation and reports are on file, accurate, and complete.
- **Study Coordination**: monitoring is conducted to assure that investigator delegation and communication with the research team is planned and systematic.

In addition to the elements noted above, the plan should also identify who is responsible for the monitoring of the data, their expertise, and if the individual or committee is independent from the research sponsor and/or the PI of the study.

At a minimum, adverse event data should be reviewed by the investigator. The DSMP may also include a review of data quality, participant recruitment, accrual, retention, outcome data, results of related studies that may impact the safety of participants, and procedures designed to protect the privacy of subjects.

The DSMP should also outline how often the individuals or committee will review the data, including what documentation will be maintained to demonstrate that the safety review was conducted. (Note: Keep in mind that this information will be reviewed at the time of continuing review. The IRB will want to see that the individuals/committee actually met at the intervals specified in the DSMP and associated documentation was maintained as indicated in the initial study submission.)

Who is responsible for monitoring data and safety?

The individual(s) performing data and safety monitoring will vary depending on the potential risks, complexity, and nature of the study. Behavioral research or clinical trials that involve surveys or other minimal risk activities should be monitored by the Principal Investigator.

If you are conducting a clinical trial involving an investigational product, such as an investigational drug or device, data and safety monitoring may be performed by the research sponsor, a medical monitor, or the contract research organization (CRO) responsible for various study-related activities. There may be times when monitoring will be conducted by the Office of Research Integrity. This may occur when an investigator is both the investigator and the sponsor of an FDA regulated clinical trial.

Some research is required to have a Data and Safety Monitoring Board (DSMB) or Data and Safety Monitoring Committee (DSMC), which is an independent monitoring group tasked with completing a review of study data at specified time intervals. DSMB/DSMCs are composed of members whose expertise and experience provide them the ability to identify problems that should be addressed and make recommendations to ensure the safety of research participants. Members of these boards/committees should not possess a conflict of interest with the research, including a financial interest in the outcome of the research.

When is a DSMB/DSMC necessary?

The following types of studies are either required or likely to have a DSMB:

- NIH-sponsored Phase 3 clinical trials (as well as some Phase 1 and 2)
- Large, multi-site randomized studies evaluating treatments intended to prolong life or reduce risk of a major adverse health outcome
- Controlled trials comparing rates of mortality or major morbidity
- When required by the IRB

The FDA recommends the use of a DSMB when an industry sponsored clinical trial includes:

- A study endpoint which might ethically require termination of the study at interim analysis, where a highly favorable or unfavorable finding is made
- A particular safety concern, such as administration of treatment by an invasive method (performed solely for research purposes)
- Vulnerable populations such as children, pregnant women, the elderly, terminally ill individuals, or those with diminished capacity
- Individuals at an elevated risk of death or other serious consequences, even with a study objective that addresses a lesser endpoint

Preparing the Data and Safety Monitoring Plan

Consider the following seven Human Subject Protection elements when developing a DSMP. Select the DSMP components (as identified in the table below) depending on the level of risk and the nature of the research study.

Protection Element	**DSMP Component**	**Examples of monitoring activities**
Subject safety	Specific subject safety parameters	Vital signs, weight, safety blood tests, cardiac status, anxiety, depression scores, etc.
	Frequency of subject safety observations	Weekly telephone follow-up, monthly appointments, observations of subject while in the clinical setting, etc.
	Individual responsible for safety monitoring	Principal investigator, study coordinator, safety monitor, independent monitor, or Data/Safety Monitoring Board, etc.
	Subject stopping rules - under what conditions will a subject be removed from study participation and who will make the decision?	Exclusion criteria, including adverse response to study procedures, pregnancy, stroke, cardiac irregularity, non-compliance with medication, etc. Include procedures for analysis and interpretation of data, etc.
	Study stopping rules - under what conditions will the study be modified or stopped and who will make the decision?	Unanticipated problems involving risks to subjects or others, unexplained adverse outcomes, life threatening adverse event, etc.
	Reporting mechanisms (i.e. deviations, adverse events (AE), serious adverse events (SAE), unanticipated problems involving risks to subjects or others)	Plans for reporting to IRB, FDA, Sponsor, participating sites, or Data/Safety Monitoring Board, etc.
Data integrity	Specific data elements to be reviewed	Subject inclusion criteria being met, transcription of data is accurate

		and complete, units of measure are recorded ap propriately, calculations are standardized and performed accurately, etc.
	Frequency of monitoring data, points in time, or after specific number of subjects	First 3 subjects and every 20th subject, monthly, quarterly, or annually, etc.
	Individual responsible for data monitoring	Principal investigator, study coordinator, safety monitor, independent monit or, etc.
Subject privacy	Under what conditions (time and place) will a subject be consented, interviewed, or tele phoned?	Observations of consenting process, interviewing, or clinical visit performed quarterly on 3 subjects. Request input from 5 subjects related to their experiences regarding privacy expectations, etc.
Data confiden tiality	What are the conditions that will protect the confidentiality of the data?	Check for locked file cabinets, secure electronic records, secure location where protected health information is stored, etc.
Product accou ntability	Who is responsible for obtaining, storing, preparing, administerin g, or disposing of the study drug or study device? Who is responsible for overseeing product accountabili ty?	Research Pharmacy, Principal Investigator, Central Pharmacy, Research Laboratory, Nursing, etc.
Study docume ntation	Study file management	Study File Management guidelines and checklist s for monitoring (sampling of study files annually), etc.
Study Coordin ation	Roles and responsibilities are cl arified, education needs are addressed, planned meetings or communications with documented meeting notes/minutes	Annual debriefing to determine if expectations are clear and if educational needs exist. Scheduled meetings are on calendar, and meeting outcomes are noted and available to staff, etc.